Position Statement

September 2024

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West Nile Virus

Background

West Nile Virus (WNV) is an arthropod borne flavivirus, first isolated in 1937 and widely distributed in Africa, Western Asia, Europe, the Middle East, and North and South America. The principal vectors are mosquitoes, and the principal hosts are wild birds. Humans and other animals (e.g. horses) are infected via mosquito bites. They are considered 'incidental hosts' as they do not develop sufficient viraemia to maintain transmission cycles. The incubation period of WNV in humans is reported to be 3–15 days. Most human infections are either asymptomatic (76%) or result in only mild flu-like symptoms with full recovery (24%), but 1 in 150 to 1 in 200 infected individuals may develop a more severe form of the disease which may culminate in fatal encephalitis, particularly if elderly or immunosuppressed.

WNV in the US and Canada

WNV emerged for the first time in the Northeast of the United States (US) in 1999. WNV case numbers increased in the US in following years, and WNV is now found across the whole of the US and into Canada.

In the US, WNV has been detected in 65 different mosquito species although only a few *Culex* species drive epizootic and epidemic transmission. The most important vectors are *Cx. pipiens* in the northern states, *Cx. quinquefasciatus* in the southern states, and *Cx. tarsalis* in the western states. WNV cases in the US peaked in 2003 with 9,862 human cases and 264 deaths. Thereafter there was a steady decline in cases until 2009 (720 human cases, 32 deaths and 116 presumptive viraemic blood donors). Except for 2012, when the highest number of WNV cases since 2003 was reported (5,674 human cases, 286 deaths, 703 presumptive viraemic blood donors), the number of WNV cases has remained relatively constant with the number of presumptive viraemic blood donors identified also remaining constant and high (in the region of 2000 WNV cases and 300 presumptive viraemic blood donors per annum). The SARS-CoV-2 pandemic was likely responsible for a reduced number of cases (less than 1,000) and presumptive viraemic blood donors (less than 150) in 2020 although case numbers increased to greater than 1,000 in 2021, 2022 and 2023, and 491 to 10 September 2024.[1]

In Canada a similar pattern has been observed. The majority (99%) of the human cases currently occur between 01 July and 31 October each year, although cases have been reported in June.[1]

As travel to the USA and Canada is common in UK blood donors, a deferral policy for such donors was adopted by UK Blood Services in June 2003 as a precautionary measure.

WNV in Europe

In Europe, sporadic WNV outbreaks have occurred in Romania (1996 and 2008), Russia (1999), Israel (2000) and Hungary (2008). During 2010, human cases were reported in several European countries, including Hungary, Spain, Italy, Greece, Romania and Russia. Whereas WNV lineage 1 is the circulating genotype in the US, both lineage 1 and lineage 2 are circulating in Europe and the importance of the presence of both lineages in Europe needs to be better understood. Further WNV outbreaks in an increasing number of areas within Europe in 2010/11 led to the recommendation for WNV nucleic acid technology (NAT) testing in the 'WNV Preparedness Plan' for countries to maintain a sufficient blood supply and a number introduced WNV NAT testing.

Monitoring of cases of WNV with weekly surveillance updates is carried out by the European Centre for Disease Prevention and Control (ECDC) (Table 1, Figure 1). Distribution of outbreaks in equids and/or birds are also monitored to indicate areas at risk for human WNV infections and in January 2022, a WNV lineage 2 infection was detected in a goshawk in Italy suggesting continuous WNV circulation and supporting overwintering of the virus.[2] The impact of climate change on geographical distribution of WNV transmission has been predicted to increase.[3]

Table 1. Locally acquired WNV cases in EU and EEA surrounding countries by year (2013-2024)[4,5]

Year	Cases in EU/EEA countries	Cases in EU-neighbouring countries
2013	228	557
2014	75	136
2015	122	193
2016	226	267
2017	201	84
2018	1549	580
2019	425	53
2020	319	17
2021	141	18
2022	1108	228
2023	709	19
2024 (to 04 Sept)	718	not reported

After a sharp increase in WNV infections in Europe in 2018 (a year in which infection numbers exceeded the total number from the previous seven years) numbers of reported WNV infections decreased. Low case numbers were reported in 2019, 2020 and 2021, likely due to pandemic lockdown arrangements and redirection of public health resources. Between 2012 and 2021, 16 EU/EEA countries reported WNV infections in both humans and animals with France, Slovakia, Germany, Spain and the Netherlands

reporting their first locally acquired WNV infections between 2018 and 2020. Since 2020, no new European countries with WNV cases have been identified although spread has been seen within countries already with a WNV risk.

The first European WNV case in 2023 was reported in week 29 (July) although, in recent years (2020 and 2021) cases were first reported in June (disease onset in week 23 and 24 respectively) with the last cases reported in November (week 43). Between the beginning of the 2024 transmission season, and as of 04 September 2024, 16 EU/EEA countries have reported 718 human cases of WNV infection with the first case being reported in March in Seville (Spain).[6] However, this case was considered sporadic, and no further cases were reported from the area at the time. Subsequent cases in Europe were reported from June onwards.

In 2017, seven Austrian blood donors from Austria were reactive for WNV during blood screening. However, follow-up investigations revealed that six of these were in fact infected with a related virus, Usutu virus (USUV). Since then, WNV blood donor screening/research studies have identified USUV infections in blood donors in Austria, Italy, Germany and the Netherlands. SACTTI has a risk assessment for USUV which is reviewed and updated regularly.

Transmission through donated products

During the 2002 epidemic in the USA, 23 patients were confirmed to have acquired WNV through transfusion of red cells, platelets or fresh frozen plasma. A case of transfusion-transmitted WNV infection from a mini-pool NAT (MP-NAT) non-reactive donation collected just before triggering conversion to individual donation NAT (ID-NAT) was reported in the US in 2016. This was deemed a rare event recognised once in 84 million donations.

A European risk model (EUFRAT) allows the calculation of an estimated number of infected blood products (throughout Europe) from donors that were infected whilst travelling to outbreak-affected areas in Europe. Even using data from the year of highest incidence (2018) it was estimated that non-compliance to European regulations (donor testing or deferral) would have resulted in 7.4 (95% CI 4.7–11.1) infected blood components from infected travelling donors throughout Europe.[7] Therefore, the risk of transmission through infected blood components in the UK from travelling donors is extremely low. The risk of WNV transmission by a local outbreak was two orders of magnitude higher (113 times) than transmission by travelling donors.

Transmission has also been reported following organ transplantation from a donor who initially acquired the infection through a blood transfusion. Several reports indicate that WNV transmission through solid organ transplantation can occur from donors who are seropositive for WNV (IgM and IgG antibodies) and WNV NAT negative but there had been no such reports of transmission from blood donations. In general, the risk of transmission by transfusion relates to a few days of viraemia starting 1–3 days after infection. Viraemia lasts a mean of six days although can take up to 104 days to clear.

WNV in the UK

There have been several human WNV cases reported in the UK. In 2006 a member of the armed forces stationed in Canada was diagnosed with WNV infection on his return to the UK, and in 2007 a Canadian resident became ill when visiting the UK. The first two cases of imported WNV in Scotland were reported in 2014, both from endemic countries outside the EU. In 2017, one case of WNV was imported into the UK (out of South Africa), four in 2018 (out of Hungary and North America) and one case in 2019. No indigenous cases of WNV have been reported in the UK.[8]

In 2010 the mosquito *Cx. modestus*, largely responsible for transmission of WNV between birds, horses and humans, in Southern Europe, was reported in the UK. The map below shows where these mosquitoes have been detected. To date *Cx. modestus* has not been detected elsewhere in England.

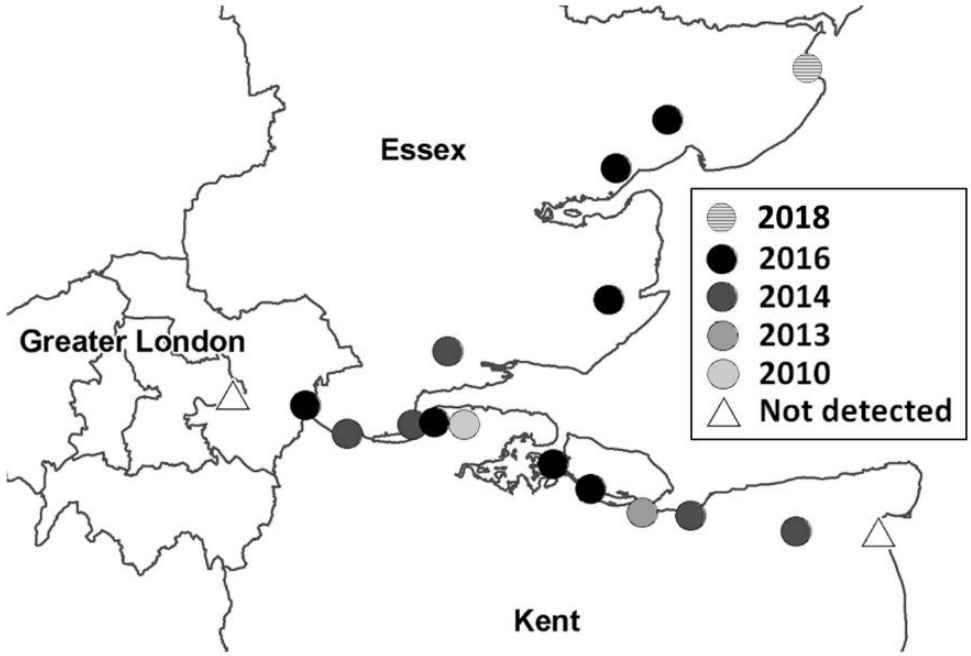

Figure 2. Map showing known distribution of Culex modestus mosquitoes in south-east England.[9]

Since the UK Blood Services' implementation of WNV NAT testing for blood donors with relevant travel history (2012–2023), no donors have been confirmed positive for WNV RNA (more than 456,000 donors tested).

UK Blood Services WNV risk reduction strategies

The EU Blood Safety Directive (and the Blood Safety and Quality Regulations 2005) requires that travellers from an area with ongoing transmission of WNV in humans should be deferred for 28 days. Originally there was no provision within the Directive for WNV NAT testing in place of deferral, as a strategy for travellers returning from an affected area. The Directive became UK statutory law as the Blood Safety and Quality Regulations 2005. Thereafter, UK Blood Services deferred travellers returning from areas at risk* of WNV. In 2012 a review of the 'WNV Preparedness Plan' agreed that WNV NAT testing could be applied by blood establishments in non-affected areas to donations from travellers returning within 28 days from an affected area if donor deferral would threaten the sufficiency of the blood supply. A 2014 amendment to the EU Blood Safety Directive supported this stance.

* A WNV risk area is defined as any part of North America (USA and Canada) or any other area with ongoing transmission of WNV ('affected area') that does not attract a malaria travel deferral of four months, and which meets the definition accepted by the European Commission/European Centre for Disease Control.

The defined WNV risk period is between 01 May and 30 November.

Donors with a history of WNV and/or a positive WNV NAT should be temporarily deferred pending investigation but may be returned to the donor panel six months after pick-up without the need for any further testing.

Solvent detergent (SD) treatment is a pathogen reduction method for plasma. WNV appears to be one of the most rapidly inactivated viruses studied although no specific inactivation data is available for SD treatment. However, other enveloped viruses such as HCV and HIV have been shown to be inactivated by $>5^{10}$ and $>6^{10}$ logs respectively. Therefore, SD treatment should also provide protection against WNV.

Information about international outbreaks of WNV is available from the National Travel Health Network and Centre (NaTHNaC).[10] Countries affected by WNV and any applicable time limits are available on the JPAC website, shown in the GDRI[11] and any associated Change Notifications.[12]

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